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ORIGINAL ARTICLE

Occupation and the risk of lung cancer by histologic types and morphologic distribution: a case control study in Turkey

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ABSTRACT: *Occupation and the risk of lung cancer by histologic types and morphologic distribution: a case control study in Turkey. O.C. Elci, M. Akpinar-Elci, M. Alavanja, M. Dosemeci.*

Background. The lung cancer incidence rate in Turkey has been increasing since the early 1980's. Etiology of lung cancer could be affected by differences in lifestyle, working conditions, and occupational exposures.

Objectives. A hospital based case-control study was conducted in Turkey to provide information on the role that occupation plays in lung cancer etiology and the relationship between occupations and histologic types and the morphologic distribution of lung cancer.

Methods. A total of 1,354 male cases and 1,519 controls were analysed. Basic information was obtained from patients from a standardised questionnaire. Occupational titles of the subjects were classified by standard occupational and industrial codes. Age- and smoking- adjusted odds ratios (OR) and 95% confidence intervals (CI) were calculated.

Results. Excess lung cancer occurred among firefighters (OR: 6.8, CI: 1.3-37.4), drivers (OR: 1.4, CI: 1.1-2.0), textile workers (OR: 1.7, CI: 1.1-2.7), water treatment plant workers (OR: 2.2, CI: 1.1-4.3) and highway construction workers (OR: 1.5, CI: 1.0-2.5). Workers in the textile and grain milling industries were shown to have a significant excess risk of squamous cell carcinoma. Textile workers, and those working at water treatment plants had excess risk of small cell carcinoma. Construction workers had excess risk of adenocarcinoma. Firefighters and workers at textile plants, grain mills, water treatment plants, and in steel production were exposed to a high risk of peripheral tumors while the risk of central tumors was excessive among drivers and highway construction workers.

Conclusions. The risk of lung cancer was associated with several occupations and peripheral located tumors and squamous lung cancer was the most common type.

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Keywords: Occupation, bronchial carcinoma, exposure, histopatology.

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Introduction

The lung cancer incidence rate in Turkey has been increasing since the early 1980's [1], and smoking is the leading causal factor [2, 3]. The International Agency for Research on Cancer (IARC) showed that lung remains an important cancer site in Turkey with the age standardized incidence rate of 35.8 per 100,000 among men, which is close to the world population rate (37.5 per 100,000) [4]. Lung cancer is strongly related to tobacco consumption, but occupational and environmental factors also play a role [5-7]. DOLL and PETO have suggested that almost one-sixth of lung cancers in men could be attributed to occupational factors [8]. Base on data from *in vitro* and animal experiments, hundreds of occupational agents has been identified as possibly carcinogenic to the lung [9].

A few studies have been carried out, investigating the occupational risk factors of lung cancer together with histologic types and morphologic distribution in developing countries where occupational exposures tend to be higher than in developed countries [10-13]. Lung cancer etiology in Turkey could be affected by differences in lifestyle, working conditions, and occupational exposures. This hospital-based case-control study was the first investigation conducted in Turkey to evaluate the association between occupational factors and lung cancer risk based on histologic types and morphologic localization of tumors.

Methods

The study population included patients from an oncology treatment centre in the Social Security Agency, Okmeydani Hospital, which is one of the largest cancer therapy centres in Turkey. It provides treatment to workers in the Marmara region, including Istanbul the biggest city, is the most industrial part of the country. Upon admission to the hospital, all patients completed a standard questionnaire administered by trained interviewers seeking information on occupational history and tobacco use. Details of the data collection method have been explained elsewhere [2,14]. Among the 7,631 cancer cases admitted to this hospital from 1979 to 1984, there were 1,390 primary lung cancer cases including 1,368 males and 22 females.

An oncologist from the hospital reviewed the records of cases for diagnostic verification and classification by World Health Organization Histologic Classification of Lung and Pleural Tumors [15]. There were 570 squamous cells (42.1%), 193 small cell (14.2%), 51 large cells (3.8%), 43 adenocarcinomas (3.2%), and 55 other types of lung cancers (4.1%). Histologic types of 442 (32.6%) cases were missing and those were excluded during the analysis of histopathologic types of lung cancer. The Morphologic distribution of tumors was coded according to the International Classification of Diseases for Oncology (ICD-O) classification system. [16] Because of the small numbers, cases with tracheal (ICD-O code 162.0) and main bronchial (code 162.2) tumors were combined (n = 136, 10.0%) and compared with peripheral tumors (codes 162.3, 162.4, 162.5 and 162.9, n = 1218, 90.0%).

Due to the small number of cases (n = 22) women were excluded from the analysis. All those women were blue-collar workers including textile workers (31.8%) and cleaners and janitors (22.7%). People with incomplete information on age, smoking, job title, industry title and ICD-O coding were also excluded, leaving 1,354 lung cancer cases and 1,519 other male cancer controls. All patients with Hodgkin's disease (n = 202), soft tissue sarcoma (n = 130), and cancers of non-melanoma skin (n = 657), testis (n = 219), bone (n = 66), male breast (n = 34), and a small series of non-cancer subjects (n = 211) admitted to the hospital during the period 1979-1984 were included in the control series. These cancer and non-cancer patients were selected for this analysis because they had the same socio-demographic background as lung cancer patients but were thought not to share similar etiologic factors with lung cancer including smoking. The two hundred and eleven non-cancer patients, included as controls, were initially misdiagnosed as having cancer and were admitted to the Okmeydani hospital for treatment. While at the hospital they were re-evaluated and diagnosed with benign pathologies.

Occupations and industries were coded using a modification of the four-digit Standard Occupational Classification (SOC) and Standard Industrial Classification (SIC) coding system used in the United States [17]. Expanded 7-digit SOC and SIC codes were created to provide more detailed information on jobs and industries. For example, "assemblers" (SOC code = 7720), one of the largest occupational groups, includes automobile assemblers (modified SOC code = 7720-018), box makers (modified SOC code = 7720-118), as well as others.

All the occupational and industrial groups with four or more cases were selected for analysis. Unconditional logistic regression analysis was used to determine odds ratios (OR) and 95% confidence intervals (CI) adjusted for age and smoking (ever/never) using SPSS version 10.0.

The pack years information was missing for up to 50% of the individuals who reported smoking, so ever/never data was then used to control for information taken from analyses presented in this paper. The ever/never ORs for lung cancer did not differ from those with pack years information vs. those without pack years information.

Results

We calculated age- and smoking-adjusted ORs for all occupations and industries with four or more cases of lung cancer: the total was 27 occupations and 30 industries. Three occupations had an excess risk of lung cancer: firefighters; textile workers; and drivers. Industries with an excess risk for lung cancer were water treatment plants and highway construction. Building cleaners were the only occupational group with deficit risk of lung cancer (table 1).

Histopathologic distribution of lung cancer by occupations and industries is presented in table 2. Textile workers had an excess risk for squamous cell carcinoma. The risk of squamous cell carcinoma also occurred in excess among workers in the grain milling industry. Textile workers had an increased risk for small cell carcinoma, as did workers at water treatment plants. Construction workers were the only group with excess risk for adenocarcinoma. No occupational or industrial group was found to have a significantly decreased risk of any histologic subgroup of lung cancer.

The age- and smoking-adjusted risks of morphologic types of lung cancer by occupations and industries are presented in table 3. Firefighters, textile workers, and workers in grain mills, water treatment plants, and steel production industries had high risks for peripheral tumors. The risk for trachea and main bronchus tumors was elevated for drivers and highway construction workers.

Discussion

In this study the smoking- and age-adjusted risk of lung cancer was significantly elevated among firefighters, textile workers, drivers, workers in the water treatment plants, and highway construction workers. Earlier studies have reported occupational and environmental factors concerning the etiology of lung cancer [6, 7]. STAYNER and WEGMAN have discussed the importance of histologic types considered in studies of occupational lung cancer and advised that future studies should give greater attention to histologic type [18]. Also PEZZOTTO and POLETTO noticed the importance of studies from developing countries due to potentially higher occupational and environmental exposure levels [13]. Differences in industrial technology, preventive measures, personal hygiene, and

Table 1. - Age- and smoking-adjusted risks of lung cancer by occupation and industry*

Occupations	n	OR (95.0% C.I.)	Industries	n	OR (95.0% C.I.)
Significantly elevated risk					
Firefighters	10	6.8 (1.3-37.4)	Water treatment plants	27	2.2 (1.1-4.3)
Textile workers	48	1.7 (1.1-2.7)	Highway construction	46	1.5 (1.1-2.5)
Drivers	88	1.4 (1.1-2.0)			
Non-significantly elevated risk					
Coffee house attendants	6	9.0 (0.6-143.7)	Grain mills	18	2.4 (0.9-6.0)
Wire drawers	7	4.0 (0.7-21.9)	Coffee houses	6	2.3 (0.5-10.6)
Assemblers	8	2.6 (0.7-10.0)	Cement production	14	2.2 (0.9-5.9)
Molding workers	4	1.7 (0.4-7.2)	Copper ores	5	2.1 (0.4-11.9)
Construction workers	72	1.3 (0.9-1.8)	Paint production	11	1.9 (0.7-5.2)
Managers	41	1.3 (0.8-2.1)	Bus transportation	24	1.6 (0.8-3.1)
Bakers	33	1.3 (0.8-2.1)	Steel production	38	1.5 (0.9-2.5)
Office Clerks	36	1.2 (0.7-2.0)	Oil production	12	1.4 (0.6-3.5)
			Gasoline services	9	1.4 (0.5-4.0)
			Leather production	16	1.3 (0.6-2.8)
			Yarn mills	13	1.3 (0.6-3.1)
			Construction	76	1.2 (0.8-1.7)
			Water transportation	35	1.2 (0.7-2.0)
			Tea production	25	1.2 (0.6-2.2)
			Railroad transportation	26	1.2 (0.6-2.3)
			Glass production	7	1.2 (0.4-3.6)
Not elevated risk					
Farmers	17	1.0 (0.5-2.1)	Saw mills	6	1.1 (0.3-4.0)
Waiters	11	1.0 (0.4-2.2)	Textile mills	70	1.0 (0.7-1.4)
Laborers	29	1.0 (0.6-1.8)	Rubber production	17	0.9 (0.5-1.8)
Mechanics	44	0.9 (0.6-1.4)	Clay production	12	0.9 (0.4-2.1)
Welders	18	0.9 (0.5-1.7)	Coal mines	41	0.8 (0.5-1.2)
Lathe operators	15	0.9 (0.4-1.8)	Sugar production	11	0.8 (0.4-1.9)
Foundry workers	9	0.9 (0.4-2.3)	Electric services	14	0.7 (0.4-1.5)
Machine setup operators	8	0.9 (0.3-2.7)	Paper production	14	0.6 (0.3-1.2)
Sailors	18	0.8 (0.4-1.5)	Fabric mills	7	0.6 (0.2-1.4)
Carpenters	18	0.8 (0.4-1.6)	Ship production	19	0.5 (0.3-1.1)
Guards	56	0.8 (0.6-1.2)	Bakery	10	0.5 (0.2-1.1)
Accountants	25	0.7 (0.4-1.3)	Pharmaceutical	5	0.3 (0.1-1.1)
Extractive workers	21	0.7 (0.4-1.4)			
Electricians	14	0.6 (0.3-1.2)			
Movers & handlers	22	0.6 (0.4-1.1)			
Significantly Decreased risk					
Cleaners	28	0.6 (0.4-0.9)			

*Occupations and industries with at least four cases of lung cancer were selected for the analysis.

educational problems may increase the risk of occupational exposures in developing countries. To our knowledge this study from a developing country is one of the few that has analysed the occupational risk for lung cancer based on histologic types and morphologic location of tumor.

Risk of Lung Cancer by Occupations and Industries

Although most previous studies have not found a relationship between specific occupational factors associated with firefighters and lung cancer, [19-21] excess lung cancer risk has been reported in some others [22-24]. Firefighters are routinely exposed to hot fumes, toxic substances such as asbestos, and polycyclic aromatic hydrocarbons (PAH), hydrogen chloride, cyanide, and thermal decomposition products [25]. Acute and chronic exposure of firefighters significantly decreases their respiratory functions in a dose-response pattern [26]. Due to differences in fire fighting – such as limited use of personal protective equipment, ventilators, and limited training on exposures and risk factors –, exposure levels might be different in developing countries including Turkey. To our knowledge, there is no data available on the limitations of firefighting technology and the risk lung cancer in developing countries. However, we believe that these factors may play a role in the etiology of lung cancer.

Table 2. - Age- and smoking-adjusted risks of lung cancer by histopathologic types for selected occupations and industries*

Occupations	n	OR (95.0% C.I.)	Industries	n	OR (95.0% C.I.)
Squamous Cell Cancer					
Textile workers	21	2.0 (1.1-3.5)	Grain mills	11	3.4 (1.2-9.4)
Coffee house attendants	4	18.6 (0.8-42.5)	Cement production	6	2.5 (0.8-7.9)
Firefighters	4	6.2 (0.8-46.2)	Paint production	6	2.1 (0.6-6.9)
Molding workers	4	3.8 (0.8-19.0)	Yarn mills	7	1.8 (0.7-4.9)
Assemblers	4	3.1 (0.6-16.4)	Bus transportation	11	1.7 (0.8-3.8)
Office clerk	20	1.5 (0.9-2.8)	Water transportation	20	1.6 (0.9-2.9)
			Steel production	17	1.6 (0.8-2.9)
			Water treatment plants	9	1.6 (0.6-3.8)
			Oil production	6	1.5 (0.5-4.6)
Small Cell Cancer					
Textile workers	9	2.2 (1.0-4.8)	Water treatment plants	8	4.3 (1.8-10.3)
Managers	8	1.9 (0.8-4.3)	Steel production	7	1.8 (0.8-4.2)
Mechanics	11	1.7 (0.9-3.3)	Highway construction	7	1.6 (0.7-3.7)
Electricians	5	1.6 (0.6-4.5)	Electric services	5	0.6 (0.2-1.7)
Large Cell Cancer					
Laborers	5	2.0 (0.5-8.8)			
Adenocarcinoma					
Construction workers	7	4.5 (1.9-10.7)			

* Occupations and industries with at least four cases of lung cancer were selected.

Most previous studies have not reported an excess risk of lung cancer among textile workers; in fact, some have reported a protective effect from employment in the cotton industry [27, 28]. Cotton dust in the textile industry contains large amount of bacterial and fungal endotoxins that ENTERLINE *et al.* postulated may induce the release of tumor necrosis factor (TNF) and interferon, as well as stimulate mitogenic, and macrophage activity [29]. Excess lung cancer risks among textile workers, however, have been reported in studies from developing countries [10-12, 21] and among workers exposed to asbestos and man-made organic fibers [30]. Exposure to asbestos and man-made mineral fibres may be related to the increased risk of lung cancer by inducing a molecular oxidative stress mechanism [31]. In our study we found an excess risk of lung cancer in textile production workers, but not in the entire textile industry. This discordance may be explained by high levels of exposure to textile dust among production workers in contrast with little exposure among clerical and administrative personnel, who were not found to be exposed to excess risk, in the industry.

An elevated risk of lung cancer among drivers has been noted in the majority of previous studies [13, 24, 32, 33], but not all [34, 35]. Diesel exhaust fumes and PAH have been shown to be associated with lung cancer risk among truck drivers [5, 33]. Asbestos could also be a risk factor amongs bus and truck drivers in Turkey because they are likely to be exposed to asbestos dust since it is common practice for them to repair and replace break pads as well as other parts of their trucks.

Asbestos, silica, diesel exhaust, and PAH exposures are known lung cancer risk factors, which may play a role in the excess risk of lung cancer among workers in the construction industry [36, 37]. These occupational factors may also explain the excess lung cancer risk among highway construction workers in our study.

Risk of Histopathologic Types of Lung Cancer by Occupations and Industries

In this study, as in most other studies of lung cancer among men, squamous cell carcinoma was the most common type of lung cancer [3, 13, 18]. Excess risk for squamous cell carcinoma was seen among textile and grain mill workers. Although there is a possible risk of lung cancer for the grain industry [38], etiologic factors are unclear and should be further evaluated. Excess risk of squamous and small cell carcinoma among textile workers in this study might be explained by asbestos exposure. Although asbestos exposure is a known carcinogen, there is not any strong link between asbestos exposure and specific histologic type of lung cancer [39]. Increased small cell carcinoma risk among water treatment plant workers might be the result of exposure to chromium and radioactive substances. [5, 40].

We observed an excess risk of lung cancer among construction workers. Higher exposure of

Table 3. - Age- and smoking-adjusted risks of lung cancer by morphologic types for selected occupations and industries*

Occupations	n	OR (95.0% C.I.)	Industries	n	OR (95.0% C.I.)
Bronchus & Parenchyma (peripheral tumors)					
Coffee house attendants	6	10.5 (0.6-174.5)	Grain mill	17	2.5 (1.0-6.4)
Firefighters	9	7.0 (1.3-39.1)	Coffee houses	6	2.5 (0.5-12.0)
Wire drawers	7	4.5 (0.8-25.0)	Cement product	13	2.3 (0.9-6.3)
Assemblers	5	2.0 (0.5-8.7)	Paint production	11	2.1 (0.7-5.7)
Molding workers	4	1.9 (0.4-8.4)	Water treatment plants	23	2.0 (1.0-4.0)
Textile worker	43	1.7 (1.1-2.8)	Copper ore	4	2.0 (0.3-12.0)
			Bus transportation	21	1.6 (0.8-3.1)
			Steel production	37	1.6 (1.0-2.7)
			Oil production	12	1.6 (0.6-3.9)
			Highway construction	38	1.5 (0.9-2.4)
			Yarn mill	13	1.5 (0.6-3.5)
Trachea & Main Bronchus (central tumors)					
Textile worker	5	1.7 (0.6-4.5)	Water treatment plants	4	3.0 (0.9-9.3)
Drivers	12	1.9 (1.0-3.6)	Highway construction	8	2.5 (1.1-5.7)
Construction workers	9	1.6 (0.8-3.5)	Construction	9	1.5 (0.7-3.0)
			Railroad transportation	4	2.1 (0.7-6.3)
			Coal mine	9	1.5 (0.7-3.1)

* Occupations and industries with at least four cases of lung cancer were selected.

cement, wood dust, and asbestos among construction workers may explain the excess risk of lung cancer, particularly adenocarcinoma. Previous studies have suggested a link between adenocarcinoma of the lung and occupational exposures including wood dust, cement dust, and asbestos exposures, but the studies had been limited by small sample size or inadequate source of pathologic materials [18, 24, 41].

Risk of Morphologic Location of Lung Cancer by Occupations and Industries

Eighty percent of the lung cancers in this study were peripheral tumors that were excessive among firefighters, textile workers, and workers in grain mills, water treatment plants, and steel production industries. Although asbestos related lung tumors tend to occur more often in peripheral sites, other chemical and physical factors may also play a role among these occupational and industrial groups [5].

Excess risks of central tumors were noted among drivers and highway construction workers. These are occupations with potential exposure to inert dust, including agents such as silica and metal dust. Previous studies have concluded that exposure to metal dusts such as chromium, nickel [42], and silica [43], increase the risk of central localised lung tumors.

Strengths and Limitations

The absence of detailed exposure information and the lack of histopathologic diagnosis in some cases (32.6%) can be seen as limitations of this study. These cases were excluded from the analysis of histopathologic types of lung cancer, but included in overall and morphologic type analyses. Since the distribution of demographic variability is similar for those with and without histopatology, we believe there is little chance for bias. One might consider the data collected between 1979 and 1984 as a limitation. Unfortunately there is no evidence that working conditions improved or those possible risk factors for lung cancer, including smoking habits have changed in Turkey over the last 25 years. We believe that current workers are still carrying at least similar occupational risk factors, as they did in the 1970's.

The large number of lung cancer cases allowed us to investigate the relationship between lung cancer and occupation in Turkey, which may have higher occupational exposure levels than in developed countries. The availability of smoking information gave us a chance to adjust ORs for smoking, at least based on ever/never data. We do not believe that there was a possibility of respondent bias for smoking data, because in Turkey, smoking is not considered a social stigma and smoking status does not affect legal status or benefits of workers. Also we excluded all smoking-related diseases from control groups.

To summarise, in this first study in Turkey, we found elevated risk of lung cancer among firefighters, drivers, and textile, water plant treatment, and highway construction workers. Squamous cell carcinoma was the most common histologic type of lung cancer, and most of these occupational groups had a high risk for peripheral tumors. Future studies of lung cancer in developing countries should evaluate the relationship between occupational exposures and lung cancer with more detailed exposure assessment methods.

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